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Enforceability Aspects for RACT (Reasonably Available Control Technology) for the Chemical Synthesis Pharmaceutical Industry

PEDCo-Environmental, Inc., Cincinnati, OH

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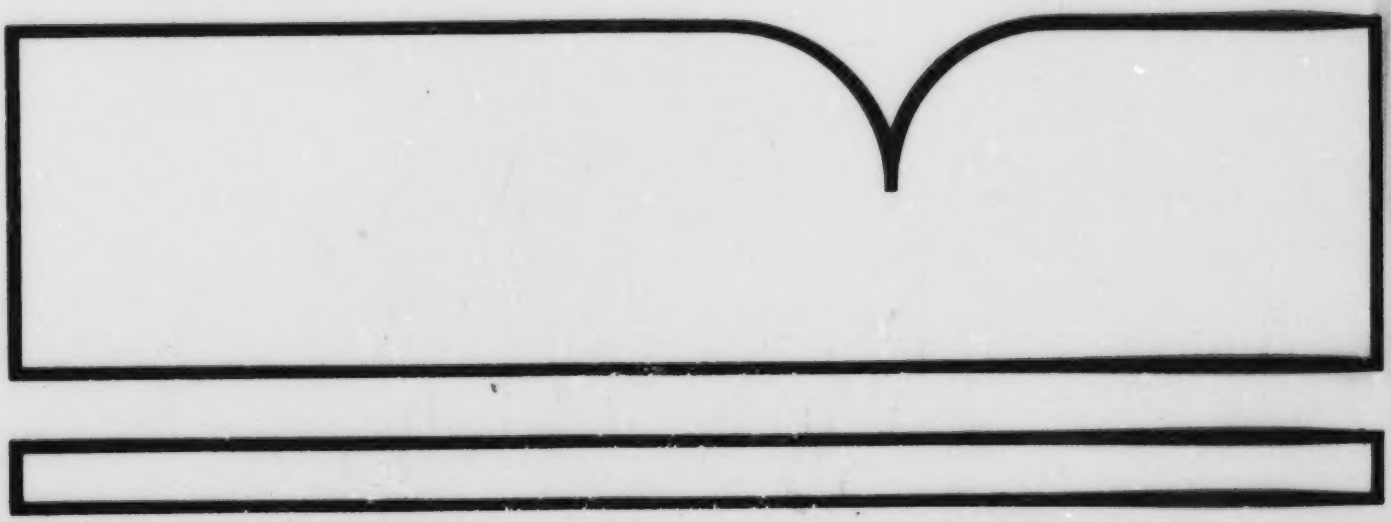

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16. ABSTRACT

Reasonably available control technology (RACT) requirements apply to pharmaceutical manufacturing plants using synthesis processes that emit more than 15 pounds per day of volatile organic compounds (VOC) located in photochemical oxidant nonattainment areas. There are 140 operating pharmaceutical plants that use chemical synthesis processes in the 10 U.S. Environmental Protection Agency regions; 116 of these are located in nonattainment areas. A current survey of the operating synthetic pharmaceutical manufacturing plants is necessary for the enforcement of RACT and for long-range planning of EPA, regional, and local programs and resources. This report provides an inventory of the operating synthetic pharmaceutical manufacturing plants, an industry process description, a review of the RACT requirements, and an evaluation of the model regulations to identify enforceability problems.

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CONTENTS

		Page
1	Introduction	1
	Background of RACT	1
	Purpose and Scope of Report	1
2	Industry Characterization	2
	Overview of Pharmaceutical Industry	2
	Process Description of Synthetic Pharmaceutical Industry	2
	Geographical Distribution of Synthetic Pharmaceutical Industry	9
3	Control Techniques and Factors Affecting Enforcement	13
	Summary of RACT Regulations	13
	Control Technologies	14
	Factors Affecting Enforcement	16
4	Recommendations For Further Investigation	19
	Determining VOC Emissions	19
	Clarifying the Bubble Concept	19
	Extending Compliance Schedules	19
Appendix A		A-1
Appendix B		B-1

TABLES

Number		Page
1	Distribution of Synthetic Pharmaceutical Manufacturing Plants by EPA Regions	10
2	Distribution of Synthetic Pharmaceutical Manufacturing Plants by States	11

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SECTION 1
INTRODUCTION

BACKGROUND OF RACT

The Clean Air Act Amendments of 1977 (CAAA) required each state to report compliance status with National Ambient Air Quality Standards (NAAQS) to the U.S. Environmental Protection Agency (EPA). Attainment and nonattainment areas of major pollutants in each state were listed in the Federal Register on March 3, 1978. According to CAAA, nonattainment areas must achieve compliance with NAAQS by December 31, 1982, with some possible extensions to 1987. Those industries in areas where standards for a particular pollutant are not being met will be required to apply Reasonably Available Control Technology (RACT) under the State Implementation Plans (SIP). The RACT requirements are based on the lowest emission limit that a particular source is capable of meeting by the application of control technology that is reasonably available in terms of technological and economic feasibility.

The RACT requirements for control of hydrocarbon emissions are explained in the Control Technique Guidelines (CTG) series. It is necessary to limit hydrocarbon emissions in order to reduce photochemical oxidant levels. With respect to the pharmaceutical industry, RACT is applicable to those manufacturing plants using synthesis processes that emit more than 15 pounds per day of volatile organic compounds (VOC).

PURPOSE AND SCOPE OF REPORT

A current survey of operating plants that manufacture synthetic pharmaceuticals in oxidant nonattainment areas is necessary for the enforcement of RACT and for long-range planning of the programs and resources of EPA's Division of Stationary Source Enforcement (DSSE), regional, and local programs.

There has been little previous regulation of air pollution control activity in this industry. The first phase of this study was to compile an inventory of the pharmaceutical manufacturing plants that use synthesis processes. The inventory includes plant demographic data, a categorization of the industry by major synthetic pharmaceutical product groups, and emission and control information.

As background for results of this survey, Section 2 presents an industry process description and a review of the RACT requirements. An evaluation of proposed regulations to identify enforceability problems is presented in Section 3; conclusions and recommendations are given in Section 4.

SECTION 2

INDUSTRY CHARACTERIZATION

OVERVIEW OF PHARMACEUTICAL INDUSTRY

The pharmaceutical manufacturing industry encompasses the manufacture, purification, and packaging of chemical materials to be used as medication for humans or animals. The broad range of industry products includes natural substances from plants or animals, chemically modified natural substances, synthetically made organic chemicals, metal-organics, and wholly inorganic materials. Production activities of the pharmaceutical industry can be grouped into the following categories:

Chemical synthesis - The manufacture of pharmaceutical products by chemical synthesis.

Fermentation - The production and separation of medicinal chemicals such as antibiotics and vitamins from microorganisms.

Extraction - The manufacture of botanical and biological products by the extraction of organic chemicals from vegetative materials or animal tissues.

Formulation and packaging - The formulation of bulk pharmaceuticals into various dosage forms such as tablets, capsules, injectable solutions, ointments, etc., that can be taken by the patient immediately and in accurate amount.

Pharmaceutical manufacturers use many VOC either as raw materials or as solvents. The Pharmaceutical Manufacturers Association (PMA) obtained from 26 member companies their estimates of the 10 VOC's that were purchased in largest volumes. According to the data obtained, about 73 percent of all emissions reported are from the chemical synthesis group. Therefore, EPA is considering only the chemical synthesis group for regulation of VOC emissions.

PROCESS DESCRIPTION OF SYNTHETIC PHARMACEUTICAL INDUSTRY

Most drugs are prepared today by chemical synthesis. The Effluent Guidelines Division of the EPA has compiled a comprehensive data base, which indicates that of pharmaceutical plants manufacturing products by chemical synthesis, 80 percent of all operations are batch processes, 8 percent are continuous, and 12 percent are semicontinuous.

The basic reaction vessel for the batch process is a mixing tank with a welded bottom and a clamped-on top. It is usually equipped with a motor-driven agitator and an internal baffle. The tank, made of either stainless steel or glass-lined carbon steel, has a carbon steel outer shell suitable for either cooling water or steam. Vessels of this type are made in many different sizes, with capacities ranging from 0.02 to 11 m^3 or more. With suitable accessories, these vessels can be used in many different ways, including the mixing, boiling, and chilling of solutions. With addition of a condenser, a complete reflux operation is possible; vacuum operation is also possible. The tanks can also be used for solvent extraction and crystallizing operations.

The manufacture of synthetic pharmaceuticals consists of using one or several of these vessels to perform the various needed operations, usually in the following sequence: (a) reaction (sometimes multiple reactions); (b) product separation; (c) purification; and (d) drying. Following a specific recipe, the reactor operator or computer-controlled mechanism blends reagents; adjusts the flow rate of cooling water, chilled water, or steam; and pumps the reactor contents into other similar vessels. At appropriate process steps, solutions are pumped through filters or centrifuges into solvent recovery headers or into waste sewers.

The vessels and their auxiliary equipment are usually combined into independent process units; a large pharmaceutical plant may contain many such units. Each unit may be suitable for the manufacture of many different pharmaceutical intermediary and final compounds. Dedicated equipment is used only for extremely high-volume production.

A pharmaceutical product is usually manufactured in a campaign, in which one or more process units are used for a few weeks or months to manufacture enough of this compound to satisfy its projected sales demand. Campaigns are usually tightly scheduled, with detailed coordination extending from procurement of raw materials to packaging and labelling of the product. For variable periods of time, therefore, a process unit actively manufactures a specific compound. At the end of each campaign, the same equipment and personnel are used to make a completely different product, utilizing different raw materials, executing a different formula, and creating different wastes.

Figure 1 shows a typical flow diagram for a batch synthesis operation. At the start of a production cycle, the reactor is usually washed and sterilized. In this example, solid reactants and solvent are charged to a batch reactor equipped with a condenser (which is usually water-cooled), and VOC may be produced as products or byproducts. Any remaining unreacted solvent is removed by distillation. When the reaction and solvent removal are complete, the product is transferred to a holding tank, in which it undergoes three to four washes of water or solvent to remove any remaining reactants and byproducts. The solvent used to wash may also be evaporated from the reaction product. The crude product may then be dissolved in another solvent and transferred to a crystallizer for purification. After crystallization, the solid material is centrifuged from the remaining solvent. In the centrifuge, the product cake may be washed several times with water or solvent. Tray, rotary, or fluid-bed dryers may then be used for final product finishing.

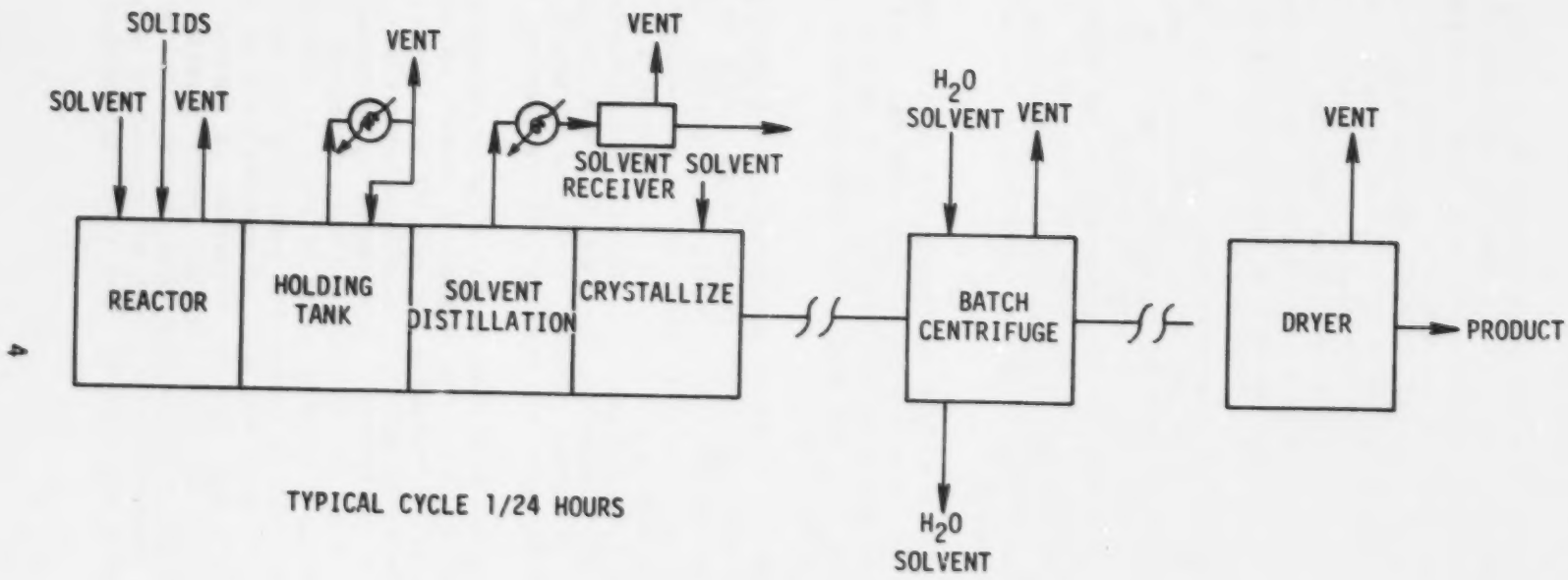

Figure 1. Typical Synthetic Organic Medicinal Chemical Process.

Organic chemicals are used as raw materials and solvents; solvents are responsible for the predominant VOC emissions from production. Almost every pharmaceutical process reaction step requires a solvent chemical to dissolve reactants and to bring them into close proximity with each other. A solvent also aids in process heat transfer and temperature control.

The synthetic pharmaceutical industry uses a wide variety of reaction and purification solvents, including water. Benzene and toluene, stable compounds that do not easily react, are the most often used organic solvents. Similar compounds such as xylene, cyclohexane, and pyridine are also used. Chlorinated hydrocarbons are used occasionally in purification operations, but are rarely used as reaction solvents.

Each operation of the chemical synthesis process may be a source of VOC emissions, which vary widely within and among operations, depending on the amount and type of VOC used, the manufacturing equipment, and the size of the operation. Because of the wide variation, typical emission rates for each operation cannot be calculated. The CTG, however, establishes an approximate ranking of emission sources, as shown below. The first four sources generally account for most of the emissions from a plant.

Dryers

Reactors

Distillation units

Storage and transfer

Filters

Extractors

Centrifuges

Crystallizers

Applicable controls for these emission sources include condensers, scrubbers, and carbon adsorbers. Use of incinerators is expected to be limited to a few specific applications. Storage and transfer emissions can be controlled by vapor return lines, vent condensers, conservation vents, vent scrubbers, pressure tanks, and carbon adsorbers. Floating roofs may be feasible controls for large storage tanks.

Dryers

Dryers remove most of the remaining solvent from a centrifuged or filtered product. Solvent is evaporated until an acceptable level of dryness is reached. Evaporation is accelerated by applying heat and/or vacuum to the solvent-laden product or by blowing warm air around or through it. Because many products degrade under severe drying conditions, the amount of heat, vacuum, or warm air flow must be carefully controlled. Several types of

dryers are used in synthetic drug manufacture, including tray, rotary, and fluid bed dryers.

A typical tray dryer consists of a rectangular chamber containing two carts with support racks. Each rack carries a number of shallow trays that are loaded with the product to be dried. Heated air is circulated within the chamber.

A rotary or tumbler dryer consists of a revolving cylindrical or conical shell supported in a horizontal or slightly inclined position. Rotary dryers may be operated under vacuum or with hot air circulation. Rotation of the dryer tumbles the product to enhance solvent evaporation and may also perform a blending function.

A fluid bed dryer evaporates solvent by forcing heated air through the wet material. Typically, a large pan loaded with the product is placed inside the dryer, where air is blown through the bottom of the pan. The air agitates or fluidizes the product. Some product particles may be entrained in the gas stream. They are captured by a fabric filter and returned to the dryer.

A dryer is a potentially large emission source. Emission rates are highest at the beginning of the cycle and lowest at the end of the cycle. Dryer size, number of drying cycles per year, and the amount and type of solvent evaporated per cycle affect the total emissions. Emissions from an air dryer are normally greater than those from a vacuum dryer, mainly because emissions from the air dryer are dilute and more difficult to control.

Reactors

A typical batch reactor is made of stainless steel or glass-lined carbon steel. The tank is usually jacketed to permit temperature control of reactions. Generally, each is equipped with a vent, which may discharge through a condenser. Batch reactors may also be used as mixers, heaters, holding tanks, crystallizers, and evaporators.

Reactor emissions may stem from the following: (a) displacement of air containing VOC during reactor charging; (b) evaporation of solvent during the reaction cycle (reaction byproduct gases act as VOC carriers in many operations); (c) venting of uncondensed VOC from an overhead condenser during refluxing; (d) purging of vaporized VOC remaining from a solvent wash; and (e) opening of a reactor during a reaction cycle to take samples or determine reaction endpoints.

Emissions may be greater when a reactor is operated under pressure because the pressure must be relieved between cycles. This may be done by venting directly to the atmosphere or through a condenser. When the reactor is vented through an overhead condenser, care must be taken not to overload the condenser by relieving reactor pressure too rapidly. The number of batches or annual throughput will affect total emissions from the reactor.

Distillation Units

Distillation is performed by either of two principal methods. The first method is based on production of a vapor by boiling the liquid mixture and condensing the vapors without allowing any liquid to return to the still. The second method is based on the return of part of the condensate to the still so that the returning liquid is brought into intimate contact with the vapors on the way to the condenser. Either of these methods may be conducted as a batch or continuous operation.

Distillation may be performed in batch reactors, in small stills attendant to reactors, or in larger distillation columns such as may be used for waste solvent recovery. The largest distillation columns in pharmaceutical plants process around 3200 kg/h (7000 lb/h) of feed material. The distillation condensers used to recover evaporated solvents may emit VOC.

Storage and Transfer

Volatile organic compounds are stored in tank farms, in 55-gallon drums, and sometimes in process holding tanks. Capacities of storage tanks in tank farms range from about 20,000 to 110,000 liters (5,000 to 30,000 gallons). Most are horizontal tanks, although vertical tanks also are used. Process holding tanks are smaller, with capacities from 2,000 to 20,000 liters (500 to 5,000 gallons). In-plant transfer of VOC is done mainly by pipeline, but also may be done manually. Raw materials are delivered to the plant by tank truck, rail car, or in 55-gallon drums.

Emissions of VOC from storage tanks are from working losses or breathing losses. The amount of loss depends on the type of VOC stored, size of tank, type of tank, diurnal temperature changes, and tank throughput.

Filters

Generally, filtration is used to remove solids from a liquid, whether these solids are product, process intermediates, catalysts, or carbon particles (e.g., from a decoloring step). The normal filtration procedure is simply to force or draw the mother liquor through a filtering medium. After filtration, the retained solids are removed from the filter medium for further processing. Pressure filters, such as shell and leaf filters, cartridge filters, and plate and frame filters, are commonly used. Atmospheric and vacuum filters are used in some applications.

Enclosed pressure filters normally do not emit VOC during a filtering operation. The filtered liquid is sent to a receiving tank. Emissions can occur when a filter is opened to remove collected solids. Emissions can also occur if the filter is purged before cleaning. The purge gas entrains evaporated solvent and probably is vented through the receiving tank.

Highest VOC emissions are from vacuum drum filters, in which solvent is pulled through a precoated filter drum. Potential emissions are significant both at or near the surface of the drum and from the ensuing waste stream.

Extraction

Extraction is used to separate components of liquid mixtures or solutions. This process is based on differences in solubilities of the components; i.e., a solvent is used that will preferentially combine with one of the components. The resulting mixture is made up of the extract, which contains the preferentially dissolved material, and the raffinate, which is the residual phase.

The pharmaceutical industry generally utilizes two kinds of solvent extraction. In the first, the extraction takes place within the reactor. Solvent is added to the vessel, and the mixture is agitated until the material to be extracted is dissolved. The mixture is then allowed to separate into two phases, and the bottom layer is drawn off and transferred to a second vessel.

The second type of extraction takes place in a vertical column. A solvent is made to flow through the liquid mixture. Either the solvent or the mixture is dispersed before entering the column; this increases contact and promotes the extraction process. Further extraction efficiency may be gained by using a packed column.

Emissions from batch extraction stem mainly from displacement of vapor while solvent is pumped into the extractor and while the vessel is purged or cleaned after extraction. Some VOC also may be emitted while the liquids are being agitated. Column extractors may emit VOC during filling or emptying of the column or during extraction. Emissions also occur through associated surge tanks. Significant amounts of solvent may be emitted from these tanks because of working losses as the tank is repeatedly filled and emptied during the extraction process.

Centrifuges

Centrifuges are used to remove intermediate or product solids from a liquid stream. Center-slung, stainless steel, basket centrifuges are most commonly used. When the centrifuge is started, liquid slurry is pumped into it. An inert gas, such as nitrogen, is sometimes introduced into the centrifuge to avoid the buildup of an explosive atmosphere. The liquid is strained through small basket perforations, and solids are retained in the basket. The solids are then scraped from the sides of the basket; they are unloaded by being scopped through a hatch on top of the centrifuge or dropped through the bottom into receiving carts.

A large potential source of VOC emissions is the open-type centrifuge, which permits large quantities of air to contact and evaporate solvents. The trend is toward complete enclosure of the centrifuge. If an inert gas blanket is used, it will be a transport vehicle for solvent vapor. This vapor may be vented directly from the centrifuge or from a process tank receiving mother liquor.

The solids are still wet with solvent and are a source of emissions while being unloaded and transported to the next process step. A bottom unloader can minimize this problem if the solids are transferred to a receiving cart

through a closed chute and the receiving cart is covered while transporting solids.

Crystallizers

Crystallization is a means of separating an intermediate or final product from a liquid solution. This is done by creating a supersaturated solution, one in which the desired compounds will form crystals. Supersaturation may be achieved in three ways: (1) if solubility of the solute increases strongly with temperature, a saturated solution becomes supersaturated by simple cooling; (2) if solubility is relatively independent of temperature, supersaturation may be attained by evaporating a portion of the solvent; (3) if neither cooling nor evaporation is desirable, supersaturation may be induced by adding a third component to form a mixture in which the solute is considerably less soluble.

Crystallization by cooling a solution will generate little VOC emission. Crystallization by solvent evaporation increases the potential for emissions. Emissions are significant if evaporated solvent is vented directly to the atmosphere. More frequently, the solvent is passed through a condenser or a vacuum jet.

GEOGRAPHICAL DISTRIBUTION OF SYNTHETIC PHARMACEUTICAL PLANTS

It is estimated that 800 to 1200 plants in the United States manufacture pharmaceutical products, of which 140 use synthesis processes. The 140 plants are scattered through 30 states and Puerto Rico and are located in all ten EPA regions.

Geographical Distribution

More than 41 percent of the plants in the synthetic chemical industry are located in EPA Region II. New Jersey and New York have 27 and 23 plants, respectively, and each plant is in a nonattainment area for oxidants. Only the 8 plants in Puerto Rico are in attainment areas.

EPA Region V has 27 plants, 24 of which are in nonattainment areas, and Illinois has the majority with 15. Of 18 synthetic pharmaceutical plants in EPA Region III, 12 are in Pennsylvania. Sixteen of the plants in Region III are in nonattainment areas.

The remaining 37 plants (26 percent of the total) are located in the other seven EPA regions, with distribution ranging from 1 plant each in Regions VIII and X to 10 plants in Region IV. Of these 37 plants, 11 are in attainment areas for oxidants, and 26 are in nonattainment areas.

Table 1 shows the breakdown of plants by EPA region; Table 2 shows the breakdown by state. Appendix A provides a listing of all synthetic pharmaceutical plants, designating county, air quality control region, and attainment/nonattainment area status. These plants produce a variety of synthetic chemicals. Appendix B lists most of the companies and their synthetically manufactured products.

TABLE 1. DISTRIBUTION OF SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS BY EPA REGIONS

Region	Total	Number of plants	
		Attainment	Nonattainment
I	4	0	4
II	58	8	50
III	18	2	16
IV	10	6	4
V	27	3	24
VI	5	1	4
VII	9	4	5
VIII	1	0	1
IX	7	0	7
X	1	0	1
Totals	140	24	116

TABLE 2. DISTRIBUTION OF SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS BY STATE

State	Number of plants	
	Attainment	Nonattainment
Alabama	0	1
Arkansas	1	0
California	0	7
Colorado	0	1
Connecticut	0	3
Delaware	0	1
Florida	1	0
Georgia	2	0
Illinois	0	15
Indiana	3	1
Iowa	1	0
Kansas	0	2
Kentucky	0	1
Louisiana	0	1
Maryland	0	1
Massachusetts	0	1
Michigan	0	5
Mississippi	1	0
Missouri	3	3
New Jersey	0	27
New York	0	23
North Carolina	1	0
Ohio	0	1
Pennsylvania	0	12
Tennessee	1	3
Texas	0	3
Virginia	1	0
Washington	0	1
West Virginia	1	2
Wisconsin	0	1
Puerto Rico	8	0

Projected Growth

The economic outlook for the pharmaceutical industry is generally positive. Although some patent expirations and governmental efforts at cost containment may threaten the industry, the profitability of developing new products will foster the industry's interests.

In all probability, growth in dollars will exceed growth in unit volume by several percent. Dollar sales should escalate by more than 10 percent per year and possibly by as much as 12 percent. Based on a compounded rate of 12 percent, the U.S. market will grow from $9.3 billion in 1978 to more than $18 billion in 1984. This assumes an annual inflationary impact of 5 to 6 percent.

The projected growth outlook provides a strong argument for smaller companies to actively seek acquisition and merger situations. The larger companies would likely be advised to alter their operations to include joint ventures and licensed products. Leading companies could have difficulty generating from internal sources the sales volume required merely to keep pace with market growth.

SECTION 3

CONTROL TECHNIQUES AND FACTORS AFFECTING ENFORCEMENT

SUMMARY OF RACT REGULATIONS

On the basis of the control technology specified in the CTG, EPA developed a model regulation affecting emission sources of facilities manufacturing synthesis pharmaceuticals. The regulation applies to all sources of VOC, such as reactors, distillation units, dryers, storage and transfer operations, filters, crystallizers, and centrifuges, that emit 15 lb/day or more. Pharmaceutical production activities excluded from the regulation are fermentation, extraction of organic chemicals from vegetable materials or animal tissues, and formulation and packaging of the product.

The owner or operator of a facility manufacturing synthetic pharmaceuticals must reduce VOC emissions by adding suitable controls or applying maintenance practices, discussed in the following paragraphs.

Where surface condensers are to be used as the control device, the outlet gas temperature must not exceed the following values (all vapor pressures measured at 20°C):

- -25°C when condensing VOC of vapor pressure greater than 40.0 kPa (5.8 psi).
- -15°C when condensing VOC of vapor pressure greater than 20.0 kPa (2.9 psi).
- 0°C when condensing VOC of vapor pressure greater than 10.0 kPa (1.5 psi).
- 10°C when condensing VOC of vapor pressure greater than 7.0 kPa (1.0 psi).
- 25°C when condensing VOC of vapor pressure greater than 3.5 kPa (0.5 psi).

The regulation for air dryers and production equipment exhaust systems states reduction of the VOC emissions by at least 90 percent if emissions are at least 150 kg/day (330 lb/day). Otherwise, emissions shall be reduced to 15 kg/day (33 lb/day).

The owner or operator of the facility must also provide a vapor balance system or equivalent control that is at least 90 percent efficient in reducing

VOC emissions from truck or railcar deliveries to storage tanks with capacities greater than 7500 liters (2000 gallons) that store VOC with vapor pressures greater than 28.0 kPa (4.1 psi) at 20°C. Installation of pressure/vacuum conservation vents set at ±0.2 kPa is also required on all storage tanks that store VOC with vapor pressures greater than 10.0 kPa (1.5 psi) at 20°C.

All centrifuges, rotary vacuum filters, and other filters having an exposed liquid surface must be enclosed if the liquid exerts a total VOC vapor pressure of 3.50 kPa (0.5 psi) or more at 20°C. Covers must be installed on all in-process tanks that contain VOC. All observed leakage of running or dripping VOC is to be corrected the first time the equipment is off-line long enough to repair the source of leak.

Final compliance is by December 31, 1982. The owner or operator may propose an alternative compliance schedule before September 15, 1980. These dates assume promulgation on July 1, 1980. Final compliance for the alternative schedule must be achieved as quickly as possible and before the date for attainment of photochemical oxidant standards.

Continuous monitoring of the following parameters is required if add-on control equipment is used: exhaust gas temperature of all incinerators, temperature rise across a catalytic incinerator bed, and breakthough of VOC on a carbon adsorption unit. States may require other continuous monitoring or recording devices and also may request an emissions test to show compliance with this regulation. Test procedures must be consistent with the EPA Guideline Series document, "Measurement Of Volatile Organic Compounds".

CONTROL TECHNOLOGIES

The model regulation for control of VOC emissions from manufacture of synthesis pharmaceuticals is based on control techniques specified in the CTG document. Briefly, these techniques specify the use of condensers, scrubbers, carbon adsorption systems, incinerators, or a combination of controls.

Condensers

Condensers are widely used to recover solvent from reactors, distillation units, extractors, separators, and dryers. In a surface condenser, the most common type, heat is transferred across a tube wall that separates the vapor and coolant. The coolant is not contaminated with the condensed VOC; thus it may be directly reused. The type of coolant depends on the degree of cooling required and is usually either water or brine. Freon may be used to provide lower cooling temperatures.

Condensation begins when the air/vapor temperature is low enough that the vapor pressure of the VOC is equal to its partial pressure. The point at which condensation first occurs is called the dew point. As the vapor is cooled further, condensation continues and the partial pressure stays equal to the vapor pressure. The less volatile a compound, the lower the amount that can remain vaporized at a given temperature.

When the solvent vapor concentration is high, condensation is relatively easy; condensers are a less attractive control option when the gas stream is dilute or far from saturation. In such cases, considerable cooling is required to condense the VOC. Condenser performance (lower temperature limit) may also be limited if one of the condensables freezes. Frozen water or VOC on the condenser tubes or walls renders them ineffective as heat transfer surfaces. The CTG outlines a method of estimating the removal efficiency of a condenser.

Scrubbers

Scrubbers are designed to provide intimate contact between the scrubbing liquid and the gaseous pollutant which promotes mass transfer between the phases. The liquid absorbs the gas because of the preferential solubility of the gas or gases in the liquid. Absorption is important in the pharmaceutical industry because many VOC's or other chemicals used are soluble in water or in caustic or acidic solutions. Scrubbers are of the venturi, packed tower, plate or tray tower, and spray tower types. Scrubbing is applied to reduce emissions from reactors, distillation equipment, process and storage tanks, centrifuges, filters, crystallizers, dryers, and fugitive sources.

The VOC concentration in a scrubber exhaust is related to the equilibrium partial pressure of the pollutant(s) in the scrubbing medium. For a given unit, overall scrubber efficiencies are influenced by intimacy of contact between gas and liquid, operating temperature, concentration of the pollutant in the gas stream, concentration of the pollutant in the liquid scrubbing medium, and gas and liquid flow rates.

Carbon Adsorbers

Activated carbon adsorption has been found effective in controlling VOC emissions because many organics are easily adsorbed onto activated carbon. Because the adsorbed compounds have practically no vapor pressure at ambient temperatures, a carbon adsorption system is particularly suited to streams with low VOC concentrations.

Activated carbon for adsorption of organic vapors should have a sponge-like structure with a large internal surface area (500 to 1000 m^2/g). Pores within the carbon structure should be about the size of the molecules to be adsorbed. Activation of the carbon consists of subjecting it to steam and/or air at high temperatures to remove strongly adsorbed hydrocarbons by oxidation or desorption.

A carbon adsorption system initially removes almost 100 percent of a VOC contaminant; then,as saturation of the carbon progresses through the bed, the VOC will break through the bed into the system exhaust. At or before breakthrough, the carbon must be regenerated and another adsorption cycle must be started. During regeneration the VOC are desorbed with steam, warm air, inert gas, or vacuum. Stripped vapors are usually condensed or adsorbed. Possible VOC emission points are condensate receivers, water (condensed steam) drains, and wastewater treatement basins.

The amount of material adsorbed on a carbon bed depends on the type of activated carbon used; the VOC characteristics; the VOC concentration; and the temperature, pressure, and humidity of the system. Overall VOC removal efficiencies depend on the system design. Units can be designed and operated at removal efficiencies well above 90 percent. Carbon adsorbers can be used to control VOC with boiling points up to 250°C and concentrations ranging from 1 ppm to 40 percent. Maximum inlet temperature of the VOC-containing stream should not exceed 140°C.

Incinerators

Incinerators and afterburners oxidize VOC in waste gases to form carbon dioxide and water. The two types of vapor incinerators in use are thermal and catalytic.

A thermal incinerator depends on direct flame contact and high temperatures to burn the combustible materials. Supplemental fuel is required to combust dilute VOC streams. Factors that influence the efficiency of combustion are temperature, degree of mixing, residence time in the combustion chamber, and type of VOC combusted. Destruction efficiency increases as the VOC concentration or the operating temperature is increased.

A catalytic incinerator preheats a contaminated waste stream to a predetermined temperature (usually lower than in thermal incineration) and promotes further oxidation by contacting the VOC with a catalyst. The efficiency of catalytic incineration is a function of the surface area of the catalyst, catalyst type, uniformity of gas flow through the bed, VOC type, oxygen concentration, volume of gas per unit of catalyst, and operating temperature of the unit. Periodic catalyst replacement is required because efficiency decreases with use of the unit. In addition, some compounds may poison the catalyst and render it ineffective. The efficiency of a catalytic incinerator depends strongly on the amount of the catalyst in the unit. Because of the high catalyst volume required for very high conversion (>98 percent) catalytic incineration is generally uneconomical.

Incinerators are not widely used to control vapor organic emissions from synthesis drug production. The primary reasons are high operating costs, variability of waste gases that would be ducted to an incinerator, and operation by batch processes. Fluctuating flows and VOC concentrations may hamper safe and efficient operation. Heat recovery is impractical because the incinerators would be relatively small and would generally run less than 24 hours per day. In addition, some compounds such as chlorinated organics, amines, and sulfinated organics can corrode the incinerator.

FACTORS AFFECTING ENFORCEMENT

Problems related to enforcement and compliance with the model regulation include the exemption of certain manufacturing processes, the provisions regarding source size, determination of compliance schedules, and application of the bubble concept.

The model regulation specifically exempts fermentation, extraction of organic chemicals from vegetable materials or animal tissues, and formulation and packaging processes. The regulation indicates that manufacturers of pharmaceutical products by chemical synthesis emit most of the VOC in the industry, but many VOC are also used and emitted by the exempted pharmaceutical manufacturing processes. In fact, many pharmaceutical companies use more than one manufacturing process at the same facility over the course of a year. Sources should not be allowed to control VOC emissions from chemical synthesis operations at a facility that operates such processes for 3 months and to exempt VOC emissions from other processes that might operate 9 months. State permit review may solve this problem.

Recent guidance for OAQPS has begun to clarify the source size provision. The criterion of 15 lb or more of VOC emission per day applies to each vent, and not the process equipment (i.e., each reactor, distillation unit, dryer, storage and process tank, VOC transfer, filter, crystallizer, centrifuge). It does not apply to the total of emissions from all the sources in a manufacturing process. The new guidance covers vents from storage tanks, centrifuges, and filters having an exposed liquid surface.

However, for further clarification it should be reworded to apply only to sources that emit 15 lb per day after the application of air pollution control equipment. This concept also agrees with the recent redefinition of "potential to emit" in the case of Alabama Power. A policy statement is planned by OAQPS on this subject. Many sources are already equipped with state-of-art air emission controls, and mass VOC emissions may already be below the exclusion level.

Determining compliance with the regulation will be difficult because the only methods currently available to measure VOC emissions are by solvent usage and/or by correct control equipment operations. The test methods cited in the model regulation are not applicable to the emissions associated with the batch operations predominant in this industry; these emissions are intermittent and highly variable, and often occur at low velocities and low concentrations. The use of alternative methods such as calculations and audits should be defined as acceptable. Another problem is that testing and monitoring requirements specify that VOC breakthrough on a carbon bed is to be continuously monitored. The equipment for the low level of detection required can be quite expensive.

The regulation should somewhere describe a vapor balance system for reducing emissions during VOC deliveries. The type of delivery specified should not eliminate any form of transportation such as barging.

Meeting the compliance schedules may pose a problem for the pharmaceutical industry. Determining compliance status and defining a compliance program for a major synthesis pharmaceutical plant will be a lengthy task. Such a plant contains hundreds of pieces of equipment, each of which may be a VOC emission source. Moreover, a single source can be used for many processes, with wide variations in the magnitude of emissions. Simply defining the scope of the compliance effort will be a major undertaking. Compliance efforts that require a process modification must also be approved by the Food and Drug Administration and thus will require additional time to meet the compliance

schedule. The model regulations provide for compliance schedule modifications, but specific guidance for this industry is needed.

Because most synthetic pharmaceutical plants contain numerous sources, the bubble concept will be beneficial to the industry in complying with VOC regulations. It may be advantageous to allow more stringent controls on the large sources and less stringent controls on the smaller sources. All uncontrolled VOC emissions must be quantified, however, before the bubble concept can be applied.

SECTION 4

RECOMMENDATIONS FOR FURTHER INVESTIGATION

Areas where further investigation could facilitate the enforcement of VOC regulation by regional, state, and local agencies include determining VOC emissions, clarifying the bubble concept, and extending compliance schedules.

DETERMINING VOC EMISSIONS

Emissions in the synthetic pharmaceutical industry vary greatly because of the nature of batch operations and also because many chemical synthesis plants may also produce pharmaceutical products by fermentation and extraction of organic materials using the same process equipment. Emissions (particularly those subject to control by the VOC regulations) usually vary from month to month and from year to year. Guidelines should be established for a method of determining potential and controlled emissions.

CLARIFYING THE BUBBLE CONCEPT

The bubble concept is beneficial to the chemical synthesis pharmaceutical industry. Clarification is needed on an overall control efficiency that can be applied plantwide for application of the bubble concept. Presently the control strategies for reduction of VOC emissions from air dryer and production equipment exhaust systems require 90 percent reduction if VOC emissions are at least 150 kg/day or require control to 15 kg/day if VOC emissions are less than 150 kg/day. A standard percentage reduction applicable to the emission sources in the plant would enhance application of the bubble concept.

EXTENDING COMPLIANCE SCHEDULES

Process modifications may delay compliance or extend the time required to install add-on controls because the Food and Drug Administration must approve all modifications. Some guidance should be prepared for situations where compliance will be delayed by process modifications. A standard method should be established for obtaining extensions required by the need for FDA approval.

APPENDIX A

SYNTHETIC PHARMACEUTICAL PLANTS BY LOCATION

This appendix provides a listing of all synthetic pharmaceutical plants, first in a table by region; then in a table by state. The county and attainment/nonattainment area status is given.

TABLE A-1.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION I

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Connecticut	3	0	3
Maine	0	0	0
Massachusetts	1	0	1
New Hampshire	0	0	0
Rhode Island	0	0	0
Vermont	0	0	0
Totals	4	0	4

TABLE A-2.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
Connecticut			
CPC International Wallingford	New Haven	42	Nonattainment
Pfizer, Inc. Groton	New London	41	Nonattainment
Sterling Drug, Inc. Glenbrook	Fairfield	43	Nonattainment
Massachusetts			
Astra Pharmaceutical Worcester	Worcester	118	Nonattainment

TABLE A-3
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION II

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
New Jersey	27	0	27
New York	23	0	23
Puerto Rico	8	8	0
Virgin Islands	0	0	0
Totals	58	8	50

TABLE A-4.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
NEW JERSEY			
Aceto Chemical Company, Inc. Carlstadt	Bergen	43	Nonattainment
American Cyanamid Bound Brook	Somerset	43	Nonattainment
Beecham, Inc. Piscataway	Middlesex	43	Nonattainment
Ciba Geigy Corporation Summit	Union	43	Nonattainment
CPC International Lyndhurst	Bergen	43	Nonattainment
CPC International Newark	Essex	43	Nonattainment
Diamond Shamrock Corp. Harrison	Hudson	43	Nonattainment
Ganes Chemicals, Inc. Carlstadt	Bergen	43	Nonattainment
Ganes Chemicals, Inc. Pennsville	Salem	45	Nonattainment
Gulf Oil Corporation Berkeley Heights	Union	43	Nonattainment
Hexcel Corporation Lodi	Bergen	43	Nonattainment
Hoffman-LaRoche, Inc. Belvidere	Warren	151	Nonattainment
Hoffman-LaRoche, Inc. Nutley	Essex	43	Nonattainment
Hummel Chemical Company South Plainfield	Middlesex	43	Nonattainment
Merck and Company, Inc. Hawthorne	Passaic	43	Nonattainment
Merck and Company, Inc. Rahway	Union	43	Nonattainment
Miles Laboratories, Inc. Clifton	Passaic	43	Nonattainment

(continued)

TABLE A-4. (continued)

OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
NEW JERSEY (continued)			
Napp Chemicals, Inc. Lodi	Bergen	43	Nonattainment
N. L. Industries, Inc. Bayonne	Hudson	43	Nonattainment
Norda, Inc. Newark	Essex	43	Nonattainment
Rhone-Paulenc, Inc. New Brunswick	Middlesex	43	Nonattainment
Richardson-Merrell, Inc. Phillipsburg	Warren	151	Nonattainment
Southland Corporation Great Meadows	Warren	151	Nonattainment
Squibb Corporation New Brunswick	Middlesex	43	Nonattainment
Stauffer Chemical Company Edison	Middlesex	43	Nonattainment
Sterling Drug, Inc. Trenton	Mercer	161	Nonattainment
Tenneco Chemicals, Inc. Garfield	Bergen	43	Nonattainment
NEW YORK			
Accurate Chemical and Scientific Corporation Hicksville	Nassau	43	Nonattainment
Aceto Chemical Company, Inc. Flushing	New York	43	Nonattainment
Aceto Chemical Company, Inc. Long Island City	New York	43	Nonattainment
American Cyanamid Pearl River	Rockland	43	Nonattainment
American Lecithin Company Woodside	Queens	43	Nonattainment

(continued)

TABLE A-4. (continued)

OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
NEW YORK (continued)			
Arenol Chemical Corporation Long Island City	New York	43	Nonattainment
Atomergic Chemetals Corp. Plainview	Nassau	43	Nonattainment
Bristol-Myers Company Syracuse	Onondaga	158	Nonattainment
Ciba Geigy Corporation Suffern	Rockland	159	Nonattainment
DDR Pharmaceutical Corporation Copiague	Suffolk	43	Nonattainment
Eastman Kodak Company Rochester	Monroe	160	Nonattainment
E. I. DuPont De Nemours and Co., Inc. Garden City	Nassau	43	Nonattainment
General Foods Corporation White Plains	Westchester	43	Nonattainment
Heterochemical Corporation Valley Stream	Nassau	43	Nonattainment
Hexagon Laboratories, Inc. Bronx	New York	43	Nonattainment
Nepera Chemical Co., Inc. Harriman	Orange	161	Nonattainment
Norton-Norwich Products, Inc. Norwich	Chenango	163	Nonattainment
Pennwalt Corporation Buffalo	Erie	162	Nonattainment
Pfizer, Inc. Brooklyn	New York	43	Nonattainment
Polychemical Laboratories, Inc. Bronx	New York	43	Nonattainment
RSA Corporation Ardsley	Westchester	43	Nonattainment

(continued)

TABLE A-4. (continued)

OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
NEW YORK (continued)			
RSA Corporation Bronx	New York	43	Nonattainment
Sterling Drug, Inc. Rensselaer	Rensselaer	161	Nonattainment
PUERTO RICO			
Abbott Labs Barceloneta		244	Attainment
E. I. DuPont De Nemours and Company Carolina		244	Attainment
Eli Lilly and Company Carolina		244	Attainment
Merck and Company, Inc. Barceloneta		244	Attainment
Norton-Norwich Products, Inc. Manati		244	Attainment
Smith Kline Guyana		244	Attainment
Squibb Corporation Humacao		244	Attainment
Upjohn Company Arecibo		244	Attainment

TABLE A-5.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION III

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Delaware	1	0	1
Maryland	1	0	1
Pennsylvania	12	0	12
Virginia	1	1	0
West Virginia	3	1	2
Washington, D.C.	0	0	0
Totals	18	2	16

TABLE A-6.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
DELAWARE			
ICI Americas, Inc. Newark	New Castle	45	Nonattainment
MARYLAND			
Becton, Dickinson, Inc. Baltimore	Baltimore	115	Nonattainment
PENNSYLVANIA			
American Home Products Paoli	Chester	45	Nonattainment
Beecham, Inc. Myerstown	Lebanon	196	Nonattainment
Carroll Products, Inc. Philadelphia	Philadelphia	45	Nonattainment
Glyco Chemicals, Inc. Williamsport	Lycoming	195	Nonattainment
Koppers Company, Inc. Petrolia	Butler	197	Nonattainment
Merck and Company, Inc. Danville	Montour	195	Nonattainment
Pharmachem Corporation Bethlehem	Northampton	151	Nonattainment
Ruetgers-Nease Chemical Co., Inc. State College	Centre	195	Nonattainment
Smith-Kline Corporation Philadelphia	Philadelphia	45	Nonattainment
Smith-Kline Corporation Swedeland	Montgomery	45	Nonattainment
Tyler Corporation Tamaque	Schuylkill	151	Nonattainment
West Chemical Products Eighty Four	Washington	197	Nonattainment

(continued)

TABLE A-6. (continued)

OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
VIRGINIA			
Merck and Company, Inc. Elkton	Rockingham	226	Attainment
WEST VIRGINIA			
American Cyanamid Willow Island	Pleasants	179	Attainment
Monsanto Company Nitro	Kanawha	234	Nonattainment
Union Carbide Charleston	Kanawha	234	Nonattainment

TABLE A-7.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION IV

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Alabama	1	0	1
Florida	1	1	0
Georgia	2	2	0
Kentucky	1	0	1
Mississippi	1	1	0
North Carolina	1	1	0
South Carolina	0	0	0
Tennessee	3	1	2
Totals	10	6	4

TABLE A-8.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
ALABAMA			
Degussa Corporation Theodore	Mobile	5	Nonattainment
FLORIDA			
SCM Corporation Gainesville	Alachua	49	Attainment
GEORGIA			
Dow Chemical U.S.A. Gainesville	Hall	57	Attainment
Merck and Company, Inc. Albany	Dougherty	59	Attainment
KENTUCKY			
Diamond Shamrock Corporation Louisville	Jefferson	78	Nonattainment
MISSISSIPPI			
Sterling Drug, Inc. Gulfport	Harrison	5	Attainment
NORTH CAROLINA			
Burroughs Wellcome Company Greenville	Pitt	168	Attainment
TENNESSEE			
Chattem, Inc. Chattanooga	Hamilton	55	Nonattainment
Eastman Kodak Kingsport	Sullivan	207	Nonattainment
Syntex Corporation Newport	Cocke	207	Attainment

TABLE A-9.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION V

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Illinois	15	0	15
Indiana	4	3	1
Michigan	6	0	6
Minnesota	0	0	0
Ohio	1	0	1
Wisconsin	1	0	1
Totals	27	3	24

TABLE A-10.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
ILLINOIS			
Abbott Laboratories North Chicago	Lake	67	Nonattainment
A. E. Staley Manufacturing Decatur	Macon	75	Nonattainment
Chemtek Laboratories Alsip	Cook	67	Nonattainment
Dawe's Laboratories, Inc. Chicago Heights	Cook	67	Nonattainment
Douglas Laboratories, Inc. Chicago Heights	Cook	67	Nonattainment
G. D. Searle and Company Skokie	Cook	67	Nonattainment
Henkel Corporation Kankakee	Kankee	67	Nonattainment
Inolex Corporation Park Forest South	Will	67	Nonattainment
Lonza, Inc. Mapleton	Peoria	65	Nonattainment
Minnesota Mining and Manufacturing Company Cordova	Rock Island	69	Nonattainment
North American Philips Corporation Waukegan	Lake	67	Nonattainment
Organics, Inc. Chicago	Cook	67	Nonattainment
Pfanstiehl Laboratories, Inc. Waukegan	Lake	67	Nonattainment
Revlon, Inc. Kankakee	Kankakee	67	Nonattainment
Vitamins, Inc. Chicago	Cook	67	Nonattainment
INDIANA			
Eli Lilly and Company Lafayette	Tippecanoe	84	Attainment

(continued)

TABLE A-10. (continued)

OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
INDIANA			
International Minerals and Chemical Corporation Terre Haute	Vigo	84	Attainment
Pfizer, Inc. Terre Haute	Vigo	84	Attainment
Reilly Tar and Chemical Corporation Indianapolis	Marion	80	Nonattainment
MICHIGAN			
Anderson Development Company Adrian	Lenawee	125	Nonattainment
Dow Chemical U.S.A. Midland	Midland	122	Nonattainment
Hexcel Corporation Zeeland	Ottawa	122	Nonattainment
Hoffman-LaRoche, Inc. Muskegon	Muskegon	122	Nonattainment
Upjohn Company Kalamazoo	Kalamazoo	125	Nonattainment
Warner-Lambert Company Holland	Ottawa	122	Nonattainment
OHIO			
Sterling Drug, Inc. Cincinnati	Hamilton	79	Nonattainment
WISCONSIN			
Oscar Mayer and Company Madison	Dane	240	Nonattainment

TABLE A-11.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION VI

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Arkansas	1	1	0
Louisiana	1	0	1
New Mexico	0	0	0
Oklahoma	0	0	0
Texas	3	0	3
Totals	5	1	4

TABLE A-12.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
ARKANSAS			
Diamond Shamrock Corporation Van Buren	Crawford	17	Attainment
LOUISIANA			
Monsanto Company Luling	St. Charles	106	Nonattainment
TEXAS			
Dow Chemical U.S.A. Freeport	Brazoria	216	Nonattainment
E. I. DuPont De Nemours and Co., Inc. Beaumont	Jefferson	106	Nonattainment
Union Carbide Corporation Texas City	Galveston	216	Nonattainment

TABLE A-13.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION VII

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Iowa	1	1	0
Kansas	2	0	2
Missouri	6	3	3
Nebraska	0	0	0
Totals	9	4	5

TABLE A-14.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
IOWA			
Salisbury Labs Charles City	Floyd	89	Attainment
KANSAS			
Daitom, Inc. Kansas City	Wyandotte	94	Nonattainment
North American Phillips Corporation Kansas City	Wyandotte	94	Nonattainment
MISSOURI			
American Cyanamid Hannibal	Marion	137	Attainment
Mallinckrodt, Inc. St. Louis	St. Louis	70	Nonattainment
Monsanto Company St. Louis	St. Louis	70	Nonattainment
Syntex Corporation Springfield	Greene	139	Attainment
Syntex Corporation Verona	Lawrence	139	Attainment
West Chemical Products, Inc. Kansas City	Jackson	94	Nonattainment

TABLE A-15.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION VIII

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Colorado	1	0	1
Montana	0	0	0
North Dakota	0	0	0
South Dakota	0	0	0
Utah	0	0	0
Wyoming	0	0	0
Totals	1	0	1

TABLE A-16.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
COLORADO			
Shell Chemical Company Denver	Denver	36	Nonattainment

TABLE A-17.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION IX

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Arizona	0	0	0
California	7	0	7
Hawaii	0	0	0
Nevada	0	0	0
American Samoa	0	0	0
Guam	0	0	0
Totals	7	0	7

TABLE A-18.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
CALIFORNIA			
Alameda Laboratorties Los Angeles	Los Angeles	24	Nonattainment
Beckman Instruments, Inc. Palo Alto	Santa Clara	30	Nonattainment
Belport Company, Inc. Camarillo	Ventura	24	Nonattainment
Hill Brothers Chemical Company City of Industry	Los Angeles	24	Nonattainment
ICI Americas, Inc. Pasadena	Los Angeles	24	Nonattainment
International Rectifier Corporation Long Beach	Los Angeles	24	Nonattainment
Minnesota Mining and Manufacturing Company Northridge	Los Angeles	24	Nonattainment

TABLE A-19.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
IN REGION X

State	No. of plants	Plants in attainment areas	Plants in nonattainment areas
Alaska	0	0	0
Idaho	0	0	0
Oregon	0	0	0
Washington	1	0	1
Totals	1	0	1

TABLE A-20.
OPERATING SYNTHETIC PHARMACEUTICAL MANUFACTURING PLANTS
BY STATE

Name and location	County	AQCR	Status
WASHINGTON			
Stansbury Chemical Company, Inc. Seattle	King	229	Nonattainment

APPENDIX B

SYNTHETIC PHARMACEUTICAL PLANTS BY TYPE OF CHEMICAL PRODUCED

This appendix provides a listing of synthetic pharmaceutical plants and their synthetically manufactured products.

ABBOTT LABORATORIES
NORTH CHICAGO, ILLINOIS 60064

Ammonium heparin
Arsanilic acid
Butabarbital
Butabarbital, sodium
Butyl aminobenzoate
para-N,N-Dichlorosulfamylbenzoic acid
Erythromycin
Erythromycin lactobionate
Erythromycin phosphate
Erythromycin stearate
Fumagillin
Heparin
Hydrochlorothiazide
Lithium heparin
Menadione
Menadione sodium bisulfite
Methapyrilene fumarate
Methapyrilene hydrochloride
Pentobarbital, sodium
Pramoxine hydrochloride
Pentobarbital, sodium
Pramoxine hydrochloride
Sodium heparin
Succinylcholine chloride
Thiopental, sodium
Tubocurarine chloride

*Plant also manufactures 13 other chemicals.

ABBOTT LABORATORIES
BARCELONETA, PUERTO RICO 00617

Erythromycin

ACCURATE CHEMICAL AND SCIENTIFIC CORPORATION
HICKSVILLE, NEW YORK 11801

Heparin
Metrizoate, meglumine
Metrizoate, sodium

*Plant also manufactures 27 other chemicals and products.

ACETO CHEMICAL CO., INC.
FLUSHING, NEW YORK 11368

Thimerosal

*Plant also manufactures 5 other chemicals.

ACETO CHEMICAL CO., INC.
CARLSTADT, NEW JERSEY 07072

Acetylglycol salicylate
Ambutonium bromide
Aminobenzoic acid
Butyl aminobenzoate
Ethyl p-aminobenzoate
Glyceryl guaiacolate
N-(2-Hydroxyethyl) gentisamide
Isobutyl-p-aminobenzoate
Salicylic acid, 3,3,5-timethylcyclohexyl ester
Tetracaine hydrochloride

*Plant also manufactures 111 other chemicals.

ACETO CHEMICAL CO., INC.
LONG ISLAND CITY, NEW YORK 11101

Phenypropanolamine hydrochloride
Tolazoline hydrochloride

*Plant also manufactures 7 other chemicals.

ALAMEDA LABORATORIES, INC.
LOS ANGELES, CALIFORNIA 90001

Chlorpromaxine hydrochloride
Diphenoxylate
Imipramine
Phendimetrazine bitartrate
Prochlorperazine, base
Pseudoephedrine hydrochloride
Trifluoperazine hydrochloride
Triprocidine hyrdochloride

*Plant also manufactures 13 other chemicals.

AMERICAN CYANAMID COMPANY
BOUND BROOKS, NEW JERSEY 08805

Beta naphthol
Diethylcarbamazine citrate
Dithiouracil
Salicylazosul fapyridine
Sulfabenzamide
Sulfachloropyrazine, sodium
Sulfadiazine
Sulfamerazine
Sulfamethazine
Sulfamethizole
Sulfapyridine
Thiouracil
Tridihexethyl chloride
Trihexyphenidyl hydrochloride

*Plant also manufactures 151 other chemicals and products.

AMERICAN CYANAMID COMPANY
HANNIBAL, MISSOURI 63401

Chlortetracycline

*Plant also manufactures 3 other chemicals.

AMERICAN CYANAMID COMPANY
PEARL RIVER, NEW YORK 10965

Chlortetracycline hydrochloride
Cyanocobalamin (intrinsic factor concentrate)
Demeclocycline hydrochloride
Minocycline hydrochloride
Nystatin
Tetracycline hydrochloride

AMERICAN CYANAMID COMPANY
WILLOW ISLAND, WEST VIRGINIA

Chlortetracycline
Bis (m-nitrophenyl) disulfide
Choline bitartrate
Choline citrate
Choline dihydrogen citrate

*Plant also manufactures 27 other chemicals and products.

AMERICAN HOME PRODUCTS CORPORATION
PAOLI, PENNSYLVANIA 19301

Ampicillin
Ampicillin, sodium
Carphenazine maleate
Cyclandelate
Dicloxacillin, sodium
Ethoheptazine citrate
Meperidine hydrochloride
Nafcillin, sodium
Norgestrel
Oxazepam
Oxethazaine
Penicillin G, benzathine
Penicillin G, potassium
Penicillin G, proclaine
Phenoxymethylpenicillin, potassium
Promazine hydrochloride
Promethazine hydrochloride
Sodium mercaptomerin

AMERICAN LECITHIN COMPANY
WOODSIDE, NEW YORK 11377

Lecithin

*Plant also produces 2 other types of products.

ANDERSON DEVELOPMENT COMPANY
ADRIAN, MICHIGAN 49221

m-Cresyl acetate

*Plant also manufactures 25 other chemicals and products.

ARENOL CHEMICAL CORPORATION
LONG ISLAND CITY, NEW YORK 11101

Methenamine mandelate

ASTRA PHARMACEUTICAL PRODUCTS, INC.
WORCESTER, MASSACHUSETTS 01606

Etidocaine
Etidocaine hydrochloride
Lidocaine
Prilocaine
Prilocaine hydrochloride
Terbutaline sulfate

ATOMERGIC CHEMETALS CORPORATION
PLAINVIEW, NEW YORK 11803

Acetazolamide
Allopurinol
Amygpalin
Aspartic acid
Bisacodyl
Bupivacaine
Calcium phytate
Carbetapentane citrate
Carisoprodol
Chlorobutanol
Chlorothiazide
Chlorpromazine base
Diazepam
Ferrous fumarate
Flurazepam hydrochloride
Hydrochlorothiazide
Hydroxyzine hydrochloride
Iossorbide dinitrate
Lidocaine
Mefenamic acid
Mepivacaine
Oxazepam
Phenacetin
Propylthiouracil
Terpin hydrate
Thimerosal
Vitamin B_{15}, sodium salt
Vitamins (unspecified)

*Plant also manufactures 20 other chemicals and products.

BECKMAN INSTRUMENTS, INC.
PALO ALTO, CALIFORNIA 94304

Parathyroid hormone

*Plant also manufactures 51 other chemicals and products.

BECTON, DICKINSON, INC.
BALTIMORE, MARYLAND 21201

Indocyanine green
Merbromin
Phenolsulfonphthalein
Salicyl alcohol

*Plant also manufactures 6 other chemicals.

BEECHAM, INC.
PISCATAWAY, NEW JERSEY 08854

Amoxicillin
Ampicillin
Carbenicillin
Cloxacillin, sodium
Dicloxacillin, sodium
Methicillin, sodium
Ticarcillin

BEECHAM, INC.
MYERSTOWN, PENNSYLVANIA 17067

Arsanilic acid
Piperazine monhydrocloride, neutral solution

*Plant also manufactures 3 other chemicals.

THE BELPORT COMPANY, INC.
CAMARILLO, CALIFORNIA 93010

Epinephrine hydrochloride (racemic)
Epinephrine (levo)

BRISTOL-MYERS COMPANY
SYRACUSE, NEW YORK 13201

Amikacin
Amikacin sulfate
Amoxicillin trihydrate
Ampicillin, sodium
Ampicillin, trihydrate
Butrophanol tartrate
Cephapirin
Cephapirin, sodium
Cloxacillin, sodium
Dicloxacillin, sodium

BRISTOL-MYERS COMPANY (CONTINUED)

Hetacillin
Hetacillin, potassium
Hydroflumethiazide
Kanamycin sulfate
Methicillin, sodium
Mitomycin C
Oxacillin, sodium
Phenethicillin, potassium
Phenoxymethyl penicillin, potassium
Phenyltoloxamine citrate
Rolitetracycline nitrate
Tetracycline
Tetracycline hydrochloride
Tetracycline phosphate complex

BURROUGHS WELLCOME CO.
GREENVILLE, NORTH CAROLINA 27834

Allopurino
2-Amino-6-Benzylthiopurine
6-Anilinopurine
Bethanidine sulfate
Busulfan
Butoxamine hydrochloride
6-Carboxypurine
6-Chloropurine
6-Cyanopurine
2, 6-Diaminopurine
Diaveridine
Digoxin
6-Dimethylaminopurine
6-Iodopurine
Mercaptopurine
6-Mercaptopurine riboside
6-Methylmercatopurine
Pyrimethamine
Thoguanine
Thiopurino
Trimethoprim
Triprolidine

*Plant also manufactures 1 other chemical.

CARROLL PRODUCTS, INC.
PHILADELPHIA, PENNSYLVANIA 19132

Allantoin
Allantoin N-acetyl DL-methionine
Allantoin polygalacturonic acid

*Plant also manufactures 7 other chemicals.

CHATTEM, INC.
CHATTANOOGA, TENNESSEE

Aminoacetic acid
Dihydroxy aluminum aminoacetate
Theophylline sodium gylcinate

*Plant also manufactures 13 other chemicals.

CHEMLEK LABORATORIES, INC.
ALSIP, ILLINOIS 60658

Calcium pantothenate (racemic)
Calcium pantothenate (racemic) calcium chloride complex

*Plant also manufactures 1 other chemical.

CIBA-GEIGY CORPORATION
SUFFERN, NEW YORK 10901

Acenocoumarol
Biscodyl
Carbamazepine
Chlorquinaldol
Chlorthalidone
Chlorthalidone and reserpine
Crotamiton
Desipramine
Dipyridamole
Heptabarbital
Imipramine hydrochloride
Oxyphenbutazone
Phenmetrazine hydrochloride
Phenylbutazone
Phenylbutazone (other ingredients)
Sulfinpyrazone

CIBA-GEIGY CORPORATION
SUMMIT, NEW JERSEY 07901

Adiphenine hydrochloride
Benzonatate
Diazepam
Dibucaine
Dibucaine hydrochloride
Diiodohydroxyquin
Dimethindene maleate
Glutethimide
Guanethidine sulfate
Hydralazine
Hydrochlorothiazide
Iodobrassid
Iodochlorhydroxyquin
Methrapone
Naphazoline hydrochloride
Nikethamide
Sodium carboxymethylcellulose
Sulfachloropyridazine, sodium
Syrosingopine
Tripelennamine
Tripelennamine citrate
Tripelennamine hydrochloride

*Plant also manufactures 2 other chemicals.

CPC INTERNATIONAL, INC.
NEWARK, NEW JERSEY 07114

L-acetyle methadol
Bismuth subgallate
Bismuth subsalicylate
Calamine
Candicidin
Codeine
Codeine hydrochloride
Codeine phosphate
Codeine sulfate
Diphenoxylate hydrochloride
Ethylmorphine hydrochloride
Glyceryl guaiacolate
Gramicidin
Hydrocodone bitartrate
Iodoform
Meperidine hydrochloride
Methadone hydrochloride
Methocarbamol
Morphine alkaloid
Morphine hydrochloride
Morphine sulfate

Neomycin
Neomycin palmitate
Noscapine
Noscapine hydrochloride
Opium and derivatives
Papaverine hydrochloride
Salicylamide
Thebaine
Tyrocidine hydrochloride
Tyrothricin

*Plant also manufactures 18 other chemicals.

CPC INTERNATIONAL, INC.
LYNDHURST, NEW JERSEY

Acetaminophen
Aloin
Berberine hydrochloride
Casanthranol
Diperodon hydrochloride
Hydrastine hydrochloride
Podophyllum
Potassium estrone sulfate
Proveratrine A
Proveratrine B
Reserpine

*Plant also manufactures 9 other chemicals and products.

CPC INTERNATIONAL, INC.
WALLINGFORD, CONNECTICUT 06492

Guaiacol

*Plant also manufactures 1 other chemical.

DAITOM, INC.
KANSAS CITY, KANSAS 66106

Calcium pantothenate (dextro)

DAWE'S LABORATORIES, INC.
CHICAGO HEIGHTS, ILLINOIS 60411

Choline chloride
Menadione sodium bisulfite
Vitamin D_3

*Plant also manufactures 2 other chemicals.

DDR PHARMACEUTICAL CORPORATION
COPIAGUE, NEW YORK 11726

L-dopa

*Plant also manufactures 1 other product.

DEGUSSA CORPORATION
THEODORE, ALABAMA 36582

Methionine

*Plant also manufactures 4 other chemicals.

DIAMOND SHAMROCK CORPORATION
HARRISON, NEW JERSEY 07029

Vitamin D_3

*Plant also manufactures 3 other chemicals and products.

DIAMOND SHAMROCK CORPORATION
LOUISVILLE, KENTUCKY 40218

Amino acids
Antibiotics (unspecified)
Calcium pantothenate (racemic)
Choline chloride
Vitamins (unspecified)

*Plant also manufactures 1 other product.

DIAMOND SHAMROCK CORPORATION
VAN BUREN, ARKANSAS 72956

B-alanine
B-alanine, calcium salt
Calcium pantothenate (dextro)

DOUGLAS LABORTORIES, INC.
CHICAGO HEIGHTS, ILLINOIS 60411

Vitamin A
Vitamin D_2
Vitamin D_3

*Plant also manufactures 2 other products.

DOW CHEMICAL U.S.A
FREEPORT, TEXAS 77541

Choline chloride
Piperazine, base
Piperazine dihydrochloride
Piperazine hydrochloride

*Plant also manufactures 96 other chemicals and products.

DOW CHEMICAL U.S.A.
GAINESVILLE, GEORGIA 30501

3,5-Dinitro-o-toluamide
Mietochlopramide

DOW CHEMICAL U.S.A.
MIDLAND, MICHIGAN 48640

Aspirin
Bromoform
3,5-Dinitro-o-toluamide
Metoclopramide
Phenyl salicylate
Salicylic acid
Sodium salicylate

*Plant also manufactures 146 other chemicals and products.

E.I. Du PONT De NEMOURS
BEAUMONT, TEXAS 77704

Methionine, hydroxyanalogue, calcium salt

*Plant also manufactures 1 other chemical.

E.I. Du PONT De NEMOURS
GARDEN CITY, NEW YORK 11530

Hydrocodone bitartrate
Oxycodone hydrochloride
Oxymorphone hydrochloride

E.I. Du PONT De NEMOURS
CAROLINA, PUERTO RICO 00630

Anistotropine

EASTMAN KODAK COMPANY
ROCHESTER, NEW YORK 14613

D-α Tocopherol
D-α Tocopherol acetate
D-α Tocopherol acid succinate
Choline chloride
Phenolsulfonphthalein

*Plant also manufactures 195 other chemicals and over 6000 organic chemicals.

EASTMAN KODAK COMPANY
KINGSPORT, TENNESSEE

Cellulose, oxidized

*Plant also manufactures 101 other chemicals and products.

GANES CHEMICALS, INC.
CARLSTADT, NEW JERSEY 07072

Aminophyll
Barbital
Barbital, sodium
Butabarbital
Butabarbital, sodium
Butalbital
Butalbital, sodium
Caffeine sodium benzoate
Dimenhydrinate
Diphenhydramine hydrochloride
Ethyl p-aminobenzoate
Glutethimide
Hexobarbital
Phendimethrazine tartrate
Phenobarbital

GANES CHEMICALS, INC. (CONTINUED)

Phenobarbital, calcium
Phenobarbital, sodium
Phentermine hydrochloride
Phenlephrine
Phenlephrine, hydrochloride
Phenlpropanolamine hydrochloride
Potassium aminobenzoate
Probenecid
Propoxyphene hydrochloride
Pseudoephedrine, base
Pseudoephedrine hydrochloride
Pseudoephedrine sulfate
Sodium aminobenzoate

*Plant also manufactures 14 other chemicals.

GANES CHEMICALS, INC.
PENNSVILLE, NEW JERSEY 08070

Glyceryl guaiacolate
Phenylpropanolamine hydrochloride

*Plant also manufactures 14 other chemicals.

GENERAL FOODS CORPORATION
WHITE PLAINS, NEW YORK 10625

Caffeine, natural

GLYCO CHEMICALS, INC.
WILLIAMSPORT, PENNSYLVANIA 17701

Ichthammol

*Plant also manufactures 64 other chemicals.

GULF OIL CORPORATION
BERKELEY HEIGHTS, NEW JERSEY 07922

Benactyzine hydrochloride
Dimethoxanate hydrochloride
Glyceryl guaiacolate
Mebutamate
Mephenesin
Nylidrin hydrochloride

GULF OIL CORPORATION (CONTINUED)

Phenformin hydrochloride
3-Quinuclipinol
Tybamate

*Plant also manufactures 33 other chemicals.

HENKEL CORPORATION
KANKAKEE, ILLINOIS 60901

D-α Tocopherol
D-α Tocopheryl acetate
D-α Tocopheryl acid succinate

*Plant also manufactures 46 other chemicals.

HETEROCHEMICAL CORPORATION
VALLEY STREAM, NEW YORK 11580

Menadione
Menadione dimethylpyrimidinol bisulfite
Menadione sodium bisulfite
Vitamin K_5

*Plant also manufactures 1 other chemical.

HEXAGON LABORATORIES, INC.
BRONX, NEW YORK 10475

Aspartic acid
Brompheniramine maleate
Cetylpyridinium chloride
Chlorpheniramine base
Chlorpheniramine gluconate
Chlropheniramine maleate
Dimenhydrinate
Diphenhydramine hydrochloride
Glyceryl gluaiacolate
Homatropine
Homatropine hydrobromide
Homatropine methylbromide
Methocarbamoc
Neostigmine bromide
Neostigmine methylsulfate
Pheniramine base
Pheniramine maleate
Phentermine
Phenylephrine hydrochloride

HEXAGON LABORATORIES, INC. (CONTINUED)

Prophylhexedrine
Pyrilamine maleate
Quinidine gluconate
Quinidine sulfate
Tropine

*Plant also manufactures 10 other chemicals.

HEXCEL CORPORATION
LODI, NEW JERSEY 07644

Benzaliconium chloride
Centaliconium chloride
Cetylpyridinium chloride

*Plant also manufactures 17 other chemicals.

HEXCEL CORPORATION
ZEELAND, MICHIGAN 49464

N-Butyroyl-p-Aminophenol
Dibenzylamine
N-Lauroyl-p-Aminophenol
N-Stearoyl-p-Aminophenol

*Plant also manufactures 22 other chemicals.

HILL BROTHERS CHEMICAL CO.
CITY OF INDUSTRY, CALIFORNIA

Phenolphthalein

*Plant also manufactures 3 other chemicals and products.

HOFFMAN-LA ROCHE, INC.
BELVIDERE, NEW JERSEY 07823

Ascorbic acid
Sodium ascorbate
Sulfamethoxazole

*Plant also manufactures 2 other chemicals.

HOFFMAN-LA ROCHE, INC.
NUTLEY, NEW JERSEY 07110

Acetyl sulfisoxazole
Apocarotenal
Biotin
Canthaxanthin
B-caroten
Chlordiazepoxide Hydrochloride
Chlorprothixene
Clidinium bromide
Dextromethorphan hydrobromide
Diazepam
L-dopa
Edrophonium chloride
5-Fluorouracil
Flurazepam
Ipronidazole
Isocarboxazid
Levorphanol tartrate
Menadiol sodium diphosphate
Methyprylon
Neostigmine bromide
Nicotinyl alcohol tartrate
Ormetoprim
D-panthenol
Panthenol (racemic)
Phenazopyridine hydrochloride
Phenindamine tartrate
Phytonadione
Pyridostigmine bromide
Pyridoxine hydrochloride
Riboflavin
Fiboflavin-5'-phosphate, sodium
Sulfadimethoxine
Sulfisoxazole
Sulfisoxazole, sodium
Thiamine hydrochloride
Thiamine mononitrate
DL-α Tocopherol
DL-α Tocopheryl acetate
Triclobisonium chloride
Vitamin A acetate
Vitamin A alcohol
Vitamin A palmitate

*Plant also manufactures 7 other chemicals and products.

HOFFMAN-LA ROCHE, INC.
MUSKEGON, MICHIGAN 49442

Dyclonine hydrochloride
Thiphenamic hydrochloride

*Plant also manufactures 21 other chemicals.

HUMMEL CHEMICAL COMPANY
SOUTH PLAINFIELD, NEW JERSEY 07080

Methapyrilene
Methapyrilene fumarate
Methapyrilene hydrochloride

*Plant also manufactures 67 other chemicals and products.

ICI AMERICAS, INC.
NEWARK, DELAWARE 19711

Isosorbide dinitrate

*Plant also manufactures 1 other product.

ICI AMERICAS, INC.
PASADENA, CALIFORNIA 91109

Isosorbide dinitrate

*Plant also manufactures 7 other products.

INOLEX CORP.
PARK FOREST SOUTH, ILLINOIS 60466

Ammonium heparin
Bile acids, oxidized
Bile salts
Dehydrocholic acid
Epinephrine (levo)
Liver concentrate
Liver, desiccated
Pepsin
Sodium heparin
Trysin

*Plant also manufactures 7 other chemicals and products.

INTERNATIONAL MINERALS AND CHEMICAL CORP.
TERRA HAUTE, INDIANA 47808

Bacitracin
Bacitracin (nonmedicinal)
Bacitracin, zinc
Bacitracin, zinc (nonmedicinal)
Choline chloride
Hexetidine
Tromethamine

INTERNATIONAL RECTIFIER CORP.
RACHELLE LABORATORIES
LONG BEACH, CALIFORNIA 90801

Chloramphenicol
Chlordiazepoxide
Chlortetracycline
Doxycycline
Oxytetracycline hydrochloride
Tetracycline hydrochloride

KOPPERS COMPANY, INC.
PETROLIA, PENNSYLVANIA 16050

Resorcinol

*Plant also manufactures 8 other chemicals and products.

ELI LILLY AND COMPANY
CAROLINA, PUERTO RICO 00630

Tobramtcin sulfate

ELI LILLY AND COMPANY
LAFAYETTE, INDIANA 47902

Acetohexamide
N-Carbamoylarsanilic acid
Cephalexin monohydrate
Cephaloridine
Cephalothin
Cephalothin, sodium
Cyclopentamine hydrochloride
Dioxyline phosphate
Erythromycin
Ethinamate
Ethomoxane hydrochloride

ELI LILLY AND COMPANY (CONTINUED)

1-Ethyl-1, 4-dihydro-4-oxo-1,3-dioxolo(4,5-g)cinnoline-3-carboxylic acid
dl-4-(2-[3-(p-hydroxyphenl)-1-methylpropyl]amino)ethylcathechol, hydrochloride
Hygromycin B
Insulin
Methadone hydrochloride
Methapyrilene hydroxybenzoylbenzoate
Methimazole
Methohexital, sodium
Nortripthyline
Papaverine hydrochloride
Penicillin G, potassium
Penicillin G, procaine
Penicillin G, procaine (nonmedicinal)
Phenoxymethyl penicillin
Phenoxymethyl penicillin, potassium
2-(3-phenoxypheny) propionic acid callium salt dihydrate
Piperocaine hydrochloride
Pyrrobutamine hydrobromide
Pyrrobutamine phosphate
Tylosin
Vancomycin
Vinblastine sulfate
Vincristine sulfate

*Plant also manufactures 46 other chemicals.

LONZA, INC.
MAPLETON, ILLINOIS 61547

Niacin
Niacinamide

*Plant also manufactures 184 other chemicals and products.

MALLINCKRODT, INC.
ST. LOUIS, MISSOURI 63147

Bismuth subgallate
Bismuth subsalicylate
Calcium gluconate
Ethyl ether (medicinal)
Iodoform
Resorcinol
Zinc phenolsulfonate
Iothalamic acid
Acetaminophen
Amyl nitrate

Codeine
Codeine phosphate
Codeine sulfate
Dihydrocodeine bitartrate
Diphenoxylate hydrochloride
Ferric hydrophosphate
Ferrous fumarate
Hydrocodone bitartrate
Magnesium citrate
Morphone sulfate
Noscapine
Oxycodone hydrochloride
Oxycodone terephthalate
Phenobarbital
Thebaine
Thymol iodide

*Plant also manufactures 133 other chemicals and products.

MERCK & CO., INC.
ALBANY, GEORGIA 31701

Chlorothiazide
Hydrochorothiazide
Methyldopa
Probencid
Sulfanilamide

*Plant manufactures 2 other chemicals and products.

MERCK & CO., INC.
DANVILLE, PENNSYLVANIA 17821

Dexamethasone
Dexamethasone phosphate
Ethopabate
Hydrocortisone acetate
Hydrocortisone phosphate
Methyldopa
Penicillin G, procaine (nonmedical)
Prednisolone-tert-butylacetate
Prednisolone phosphate
Riboflavin
Ronidazone
Sulindac

MERCK & CO., INC.
ELKTON, VIRGINIA 22827

Amprolium
Carbidoda
Cefoxitin
Cyanocobalamin
Nicarbazin
Sulfaquinoxaline

*Plant also manufactures 3 other products.

MERCK & CO., INC.
RAHWAY, NEW JERSEY 07065

Amitriphyline hydrochloride
Anileridine hydrochloride
Apomorphine hydrochloride
Bethanechol chloride
Bismuth formic iodide
Cambendazole
Carbachol
Cocaine
Codeine
Cyclobenzaprine
Cyproheptadine hydrocholoride
Dichlorphenamide
Ethacrynic acid
Ethylmorphine hydrochloride
Gold sodium thiomalate
Hexaylcaine hydrochloride
Hexylresorcinol
Hydrocodone bitartrate
Indomethacin
Mecamylamine
Metaraminol bitartrate
Methacholine chloride
Methyldopate hydrochloride
Metyrosine
Monochloracetone
Morphine
Nalorphine hydrochloride
Noscapine
Oxycodone hydrochloride
p-Pentoxyphenol
Phthalysulfathiazole
Phytonadione
Protriptyline hydrochloride
Sulfabromomethazine, sodium

MERCK & CO., INC.

Thiabendazole
Timocol maleate

*Plant also manufactures 4 other chemicals and products.

MERCK & CO., INC.
HAWTHORNE, NEW JERSEY 07507

Chloromercuriphenol
Mercuric salicylate
Oxyquinoline
Oxyquinoline, citrate
Oxyquinoline, sulfate

*Plant also manufactures 13 other chemicals and products.

MERCK & CO., INC.
BARCELONETA, PUERTO RICO 00617

Methyldopa

MILES LABORATORIES, INC.
CLIFTON, NEW JERSEY

Pepsin

*Plant also manufactures 14 other chemicals.

MINNESOTA MINING AND MANUFACTURING CO.
RIKER LABORATORIES
CORDOVA, ILLINOIS 61242

Sodium heparin

MINNESOTA MINING AND MANUFACTURING CO.
RIKER LABORATORIES
NORTHRIDGE, CALIFORNIA 91324

Alkaveruir
Alseroxylone
Ammonium heparin
Calcium heparin
Chlophedianol hydrochloride
Deanol p-acetamidobenzoate
Lithium heparin

MINNESOTA MINING AND MANUFACTURING CO. (CONTINUED)

Methenamine hippurate
Orphenadrine citrate
Orphenadrine hydrochloride
Sodium heparin

MONSANTO COMPANY
LULING, LOUISIANA 70070

Acetaminophen

*Plant also manufactures 7 other chemicals and products.

MONSANTO COMPANY
NITRO, WEST VIRGINIA 25143

Methionine, hydroxy analogue, calcium salt

*Plant also manufactures 20 other chemicals and products.

MONSANTO COMPANY
ST. LOUIS, MISSOURI 63177

Aspirin
L-dopa
Methapyrilene fumarate
Methapyrilene hydrochloride
Phenacetin
Salicylic acid

*Plant also manufactures 20 other chemicals and products.

MORTON-NORWICH PRODUCTS, INC.
NORWICH, NEW YORK 13815

Aspirin
Furazolidone
Nifuralidone
Nihydrazone
Nitrofurantoin
Nitrofurazone

*Plant also manufactures 6 other chemicals.

MORTON-NORWICH PRODUCTS, INC.
MANATI, PUERTO RICO 00701

Nitrofurantoin

NAPP CHEMICALS, INC.
LODI, NEW JERSEY 07644

Aminobenzoic acid
Betaine hydrochloride
Bisacodyl
Calcium glutamate
Calcium succinate
Diiodohydroxyquin
Ethyl p-aminobenzoate
Glutamic acid hydrochloride
Iodochlorhydroxyquin
Lidocaine
Methionine
Orphenadrine citrate
Oxyquinoline
Oxyquinoline benzoate
Oxyquinoline sulfate
Phenyltoloxamine dihydrogen citrate
Phthalylsulfacetamide
Potassium glutamate
Propoxyphen hydrochloride
Resorcinol
Sodium caprylate
Sulfacetamide
Sulfacetamide, sodium
Sulfadiazine
Sulfaguanidine
Sulfamerazine
Sulfamethazine
Sulfanilamide
Sulfapyridine
Sulfathiazole
Sulfathiazole, sodium

*Plant also manufactures 10 other chemicals.

NEPERA CHEMICAL CO., INC.
HARRIMAN, NEW YORK 10926

Methenamine mandelate
Niacin
Niacinamide

NEPERA CHEMICAL CO., INC.

Phenazopyridine hydrochloride
Phenylpropanolamine hydrochloride
Thonzylamine hydrochloride

*Plant also manufactures 10 other chemicals.

N. L. INDUSTRIES, INC.
BAYONNE, NEW JERSEY 07002

Zinc undecylenate

*Plant also manufactures 36 other chemicals and products.

NORDA, INC.
NEWARK, NEW JERSEY 07114

Chlorothymoc

*Plant also manufactures 46 other chemicals and products.

NORTH AMERICAN PHILIPS CORP.
KANSAS CITY, KANSAS 66110

Choline chloride

*Plant also manufactures 8 other chemicals and products.

NORTH AMERICAN PHILIPS CORP.
WAUKEGAN, ILLINOIS 60085

Calcium pantothenate (racemic) calcium chloride complex

ORGANICS, INC.
CHICAGO, ILLINOIS 60625

Adrenocorticotropin
Estrogenic substances, conjugated
Hormones, steroid type
Natural estrogenic substance

OSCAR MAYER & CO.
MADISON, WISCONSIN 53701

Pepsin
Sodium heparin

*Plant also manufactures 1 other chemical.

PENNWALT CORPORATION
BUFFALO, NEW YORK 14240

Calcium undecylenate
Zinc undecylenate

*Plant also manufactures 7 other chemicals.

PFANSTIEHL LABORATOTIES, INC.
WAUKEGAN, ILLINOIS 60085

L-Cysteine hydrochloride

*Plant also manufactures 73 other chemicals and products.

PFIZER, INC.
BOOKLYN, NEW YORK 11206

Bacitracin
Calcium gluconate
Copper gluconate
Dihydrostreptomycin
Ferrous gluconate
Hydrocortisone
Magnesium gluconate
Oleandomycin
Potassium gluconate
Viomycin

PFIZER, INC.
GROTON, CONNECTICUT 06340

Ascorbic acid
Benzthiazide
Caffeine, synthetic
Carbetapentane citrate
Doxycycline
Hydrocortisone
Hydroxyzine hydrochloride
Hydroxyzine pamoate

Methacycline
Neomycin
Neomycin sulfate (nonmedicinal)
Oleandomycin
Oxyphencyclimine hydrochloride
Penicillin G
Penicillin G, potassium
Penicillin G, procaine
Penicillin G, sodium
Penicillin O, sodium
Phenethicillin, potassium
Phenoxymethyl penicillin
Polythiazide
Procaine hydrochloride
Pyranthel pamoate
Pyranthel tartrate
Streptomycin
Streptomycin (nonmedical)
Tetracycline
Tetrahydrozoline hydrochloride
Troleandomycin
Viomycin
Vitamin A acetate
Vitamin A alcohol
Vitamin A palmitate

*Plant also manufactures 21 other chemicals and products.

PFIZER, INC.
TERRE HAUTE, INDIANA 47808

Cyanocobalamin
Oxytetracycline (nonmedicinal)
Streptomycin (nonmedicinal)

*Plant also manufactures 3 other chemicals.

PHARMACHEM CORP.
BETHLEHEM, PENNSYLVANIA 18018

Dextran

*Plant also manufactures 4 other chemicals and products.

POLYCHEMICAL LABORATORIES, INC.
BRONX, NEW YORK 10474

Acetylcholine chloride
Calcium levulinate
Calcium phytate
N-Carbamoylarsanilic acid
Chlorpheniramine maleate
Danthron
Diiodohydroxyquin
Diphenylhydantoin, sodium
Glycobiarsol
Iodochlorhydroxyquin
Methenamine mandelate
Naphazoline hydrochloride
Oxyquineline hydrochloride
Oxyquinoline sulfate
Phtahlylsulfacetamide
Piperazine adipate
Piperazine citrate
Piperazine tartrate
Propylthiouracil
Pyrilamine maleate
Sodium arsanilate
Thimerosal

*Plant also manufactures 10 other chemicals.

REILLY TAR & CHEMICAL CORP.
INDIANAPOLIS, INDIANA 46204

Niacin
Niacinamide

*Plant also manufactures 90 other chemicals and products.

REVLON, INC.
KANKAKEE, ILLINOIS 60901

Adrenocorticotropin
Bile extracts
Chymotrypsin
Insulin
Oxytocin
Trypsin

*Plant also manufactures 15 other products.

RHONE-POULENC, INC.
NEW BRUNSWICK, NEW JERSEY 08901

Dimetridazole
Glycol monosalicylate
Metronidazole

*Plant also manufactures 11 other chemicals and products.

RICHARDSON-MERRELL, INC.
PHILLIPSBURG, NEW JERSEY 08865

Azacyclonol hydrochloride
Bismuth subgallate
Chlorotrianisene
Dicyclomine hydrochloride
Diethylpropion hydrochloride
Doxylamine succinate

*Plant also manufactures 117 other chemicals.

R.S.A. CORP.
ARDSLEY, NEW YORK 10502

Acetylcholine bromide
Acetylcholine chloride
Acetylcholine iodide
Acetyl-β-methylcholine bromide
Acetyl-β-methylcholine chloride
Aspirin, calcium salt
Butyl aminobenzoate
Dibucaine hydrochloride
Diiodohydroxyquin
Guaiacol salicylate
Hexamethonium chloride
Hexamethonium iodide
Hexylresorcinol
4-Hydroxynicotinic acid
Isobutyle-p-aminobenzoate
Methacholine chloride
Methenamine mandelate
Phenylbutazone, sodium salt
Propantheline bromide
Propyl aminobenzoate
Salicyl alcohol
Tetracaine
Tetracaine hydrochloride
Tetraethylammonium chloride

*Plant also manufactures 297 other chemicals.

RUETGERS-NEASE CHEMICAL COMPANY, INC.
STATE COLLEGE, PENNSYLVANIA 16801

Chloraminophenamide

*Plant also manufactures 18 other chemicals.

SALSBURY LABORATORIES
CHARLES CITY, IOWA 50616

Ammonium phenolsulfonate
Salicylazosulfapyridine
Sodium phenolsulfonate
Sulfanilamide
Sulfapyridine
Zinc phenolsulfonate

*Plant also manufactures 16 other chemicals.

SCM CORPORATION
GAINESVILLE, FLORDIA 32601

Acepromazine
Chlordiazepoxide
Chlorpromazine hydrochloride
5-Fluorouracil
Halothane
Promazine hydrochloride

*Plant also manufactures 60 other chemicals and products.

G. D. SEARLE & CO.
SKOKIE, ILLINOIS 60075

Aminophylcine
Dimenhydrinate
Estradiol
Ethisterone
Methyltestosterone
Spironolactone
Testosterone
Testosterone and esters

SHELL CHEMICAL COMPANY
DENVER, COLORADO 80201

2,2-Dichlorovinyl-O,O-dimethyl phosphate

*Plant also manufactures 5 other chemicals.

SMITHKLINE CORP.
PHILADELPHIA, PENNSYLVANIA 19101

Amphetamine sulfate (racemic)
Caramiphen edisylate
Chlorpheniramine maleate
Chlorpromazine, base
Chlorpromazine hydrochloride
Dextroamphetamine sulfate
Hydroxyamphetamine hydrobromide
Isopropamide iodide
Prochlorperazine, base
Prochlorperazine edisylate
Prochlorperazine maleate
Propylhexedrine
Triamterene
Trifluoperazine, base
Trifluoperazine hydrochloride
Trimeprazine tartrate

*Plant also manufactures 8 other chemicals.

SMITHKLINE CORP.
SWEDELAND, PENNSYLVANIA 19479

Cefazolin
Cephradine

SMITHKLINE CORP.
GUYAMA, PUERTO RICO

Cimetidine
Cimetidine hydrochloride

SOUTHLAND CORP.
GREAT MEADOWS, NEW JERSEY 07838

5-Chloro-8-Quinolinol
Diiodohydroxyquin
Oxyquinoline
Oxyquinoline benzoate
Oxyquinoline citrate
Oxyquinoline sulfate
Phenylpropanolamine hydrochloride
6-Methoxytetralone-1
5-nitroisophthalic acid
M-Nitro-p-phenylenediamine
4-Nitro-o-phenylenediamine

*Plant also manufactures 32 other chemicals.

SQUIBB CORP.
NEW BRUNSWICK, NEW JERSEY 08903

Amphotericin B
Bendroflumethiazide
Diatrizoate, meglumine
Diatrizoate, sodium
Diatrizoic acid
Flumethiazide
Fluphenazine hydrochloride
Insulin
Iodipamide, meglumine
Iodipamide, sodium
Neomycin
Nystatin
Nystatin (nonmedicinal)
Penicillin G, potassium
Penicillin G, procaine (nonmedicinal)
Procainamide hydrochloride
Proparacaine hydrochloride
Sincalide
Thirostrepton
Trifluprom azine

*Plant also manufactures 2 other chemicals.

SQUIBB CORP.
HUMACAO, PUERTO RICO

Cephradine
Halcinonide
Triamcinolone
Triamcinolone acetonide
Triamcinolone diacetate
Amphotericin B
Nystatin
Amoxicillin
Ampicillin
Ampicillin, trihydrate
Dihydroampicillin

A. E. STALEY MFG. CO.
DECATUR, ILLINOIS

Amino acid mixtures
Inositol
Lecithin

STANSBURY CHEMICAL CO., INC.
SEATTLE, WASHINGTON

Ephinephrine

STERLING DRUG, INC.
CINCINNATI, OHIO

Benzalkonium chloride
Gentian violet
Nalidixic acid
Salicylic acid

*Plant also manufactures 34 other chemicals.

STERLING DRUG, INC.
RENSSELAER, NEW YORK

Acetarsone
Aminacrine
Aminacrine hydrochloride
Arterenol hydrochloride (racemic)
Arterenone
Cetalkonium chloride
Cinnamylephedrine hydrochloride
Danthron
Diatrizoate, sodium
Epinephrine bitartrate (levo)
Ethacridine lactate
Isoproterenol hydrochloride
Levarterenol bitartrate, monohydrate
Lidocaine
Lidocaine hydrochloride
Mafenide hydrochloride
Mafenide hydrochloride
Meperidine hydrochloride
Mepivacaine hydrochloride
dl-Metanephrine hydrochloride
Metaraminol bitartrate
Nordefrin hydrochloride
Norepinephrine
Norepinephrine bitartrate
dl-Normetanephrine hydrochloride
Pepsin
Phenacaine hydrochloride
Phenylalanine
Phenylephrine
Phenylephrine hydrochloride
Primaquine phosphate
Quinacrine hydrochloride

STERLING DRUG, INC. (CONTINUED)

Succinylcholine chloride
Tetracaine
Tetracaine hydrochloride
Trihexyphenidyl hydrochloride
L-Tryptophan

*Plant also manufactures 17 other chemicals.

SYNTEX CORPORATION
SPRINGFIELD, MISSOURI

Allantoin
Betaine base
Calcium pantothenate (dextro)
Calcium pantothenate (racemic)

*Plant also manufactures 1 other chemical.

SYNTEX CORPORATION
VERONA, MISSOURI

β-Alanine
Bethine hydrochloride
Calcium pantothenate (racemic) calcium chloride complex
Choline bitartrate
Choline chloride
Choline dihydrogen citrate
Ethylenediamine dihydroiodide
Pantolactone

*Plant also manufactures 3 other chemicals.

TENNECO CHEMICALS, INC.
GARFIELD, NEW JERSEY

Phenyl salicylate
Potassium guaicolsulfonate
Potassium salicylate
Salicylic acid
Salicylsalicylic acid
Sodium salicylate

*Plant also manufactures 16 other chemicals.

TYLER CORPORATION
TAMAQUA, PENNSYLVANIA

Glyceryl trinitrate
Isosorbide dinitrate
Mannitol hexanitrate
Pentaerythritol tetranitrate

*Plant also manufactures 7 other chemicals.

UNION CARBIDE CORPORATION
TEXAS CITY, TEXAS

Piperaine, base
Piperazine, derivatives

*Plant also manufactures 43 other chemicals.

THE UPJOHN COMPANY
KALAMAZOO, MICHIGAN

Chlorphenesin
Colestidol
Cortisone
Cortisone acetate
Cytarabine
Cytarabine hydrochloride
Diflorasone diacetate
Diphenadione
Ephedrine hydrochloride
Ephedrine sulfate
Erythromycin
Erythromycin stearate
Estradiol cypionate
Ethisterone
Fluorocortisone acetate
Flurometholone
9-α-Fluroprednisolone acetate
Fluoxymesterone
Fluprednisolone
Hydrocrotisone
Hydrocortisone acetate
Hydrocortisone cypionate
Hydrocrotisone hemisuccinate
Hydrocortisone sodium succinate
11α-Hydroxypregn-4-ene-3,20-dione
17α-Hydroxyprogesterone
Hydroxyprogesterone caproate
Lincomycin hydrochloride
Medroxyprogesterone acetate

Melengestrol acetate
6α-Methylprednisolone
Methylprednisolone acetate
Methylprednisolone sodium succinate
Methyltestosterone
Mibolerone
Neomycin sulfate
Novobiocin
Novobiocin calcium
Novobiocin sodium
Prednisolone
Prednisolone acetate
Prednisone
Progesterone
Prostaglandins
Spectinomycin dihydrochloride
Spectinomycin sulfate
Tetracyclone hydrochloride
Tolazamide
Tolbutamide

*Plant also manufactures 15 other organic chemicals.

THE UPJOHN COMPANY
ARECIBO, PUERTO RICO

Clindamycin
Clindamycin palmitate
Clindamycin phospate
Ibuprofen
Lincomycin

VITAMINS, INC.
CHICAGO, ILLINOIS

7-Dehydrocholesterol
Vitamin D_2
Vitamin D_3

VITAMINS, INC.
MICHIGAN CITY, INDIANA

Ergosterol

*Plant also manufactures 4 other organic chemicals.

WARNER-LAMBERT COMPANY
HOLLAND, MICHIGAN

Amitriptyline
Amodiaquin
Amodiaquin hydrochloride
Bisacodyl
Bromodiphenhydramine hydrochloride
Carbromal
Chlordiazepoxide
Diphenhydramine hydrochloride
Diphenylhydantoin
Diphenylhydantoin, sodium
Ethosuximide
Ethyl-p-aminobenzoate
Ketamine hydrochloride
Meclofenamic acid
Mefenamic acid
Methsuximide
Oxolinic acid
Oxytocin
Phensuximide
Phenylpropanolamine hydrochloride
Prazepam
Procainamide hydrochloride
Procaine hydrochloride
Propylhexedrine
Salicylsalicylic acid
Thiamycal, sodium
Vasopressin

*Plant also manufactures 18 other chemicals.

WEST CHEMICAL PRODUCTS, INC.
EIGHTY FOUR, PENNSYLVANIA

Phenothiazine

*Plant also manufactures 3 other chemicals.

WEST CHEMICAL PRODUCTS, INC.
HAMILTON, NEW YORK

Dry cow injectable antibiotics
Lactating cow injectable antibiotics

WEST CHEMICAL PRODUCTS, INC.
KANSAS CITY, MISSOURI

Ethylenediamine dihydroiodide

*Plant also manufactures 2 other organic chemicals.